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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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AM 101333

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25291

7590

01/07/2009

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EXAMINER

TONGUE, LAKIA J

ART UNIT

PAPER NUMBER

1645

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/796,925	<b>Applicant(s)</b> LI ET AL.	
	<b>Examiner</b> LAKIA J. TONGUE	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's response filed on October 14, 2008 is acknowledged. Claims 22-24 are currently pending and under examination.

#### ***Rejections Maintained***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. The rejection of claims 22 and 24 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Effect of dairy calves with an inactivated *E. coli* O157:H7 bacterin on shedding of *E. coli* O157:H7, 1999; Abstract 40 aP), Saito et al. (U.S. 2005/0158330 A1), and Baylor et al. (Vaccine, 2002; 20: S18-S23) is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) The Li Declaration shows that an inactivated *E. coli* O157:H7 vaccine adjuvanted with SP oil plus aluminum hydroxide produced a markedly enhanced immune response in calves, as compared to a vaccine composition containing aluminum hydroxide only.

2) It would have been unlikely for a person of ordinary skill in the art to reconstruct the oil emulsion of the present claims based on the multiple laundry lists of ingredients presented in Saito.

3) None of the cited references teach or suggest combining an oil emulsion adjuvant with aluminum hydroxide.

4) Saito does not disclose that aluminum hydroxide is added to the W/O/W emulsion formulation.

5) Baylor refers only to the use of aluminum hydroxide by itself, there is no suggestion to combine aluminum hydroxide with any other adjuvant system.

Applicant's arguments have been considered, but are not persuasive.

The rejected claims are drawn to a method for reducing shedding of *E. coli* O157:H7 in an animal which comprises administering by parenteral injection to the animal an effective amount of a vaccine composition, wherein the vaccine composition comprises inactivated or killed *E. coli* O157:H7, an adjuvant and aluminum hydroxide, and optionally a pharmaceutically acceptable carrier; wherein said adjuvant is an oil emulsion comprising:

- a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer;
- b) 2% to 6% vol/vol of squalene;
- c) 0.1% to 0.5% vol/vol of polyoxyethylene sorbitan monooleate; and
- d) buffered salt solution.

With regard to Point 1, Applicant's assertion of unexpected results, Applicant has failed to provide evidence supporting said assertion. Applicant's claims are drawn, in

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part to an adjuvant and aluminum hydroxide; wherein said adjuvant is an oil emulsion comprising: a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer; b) 2% to 6% vol/vol of squalene; c) 0.1% to 0.5% vol/vol of polyoxyethylene sorbitan monooleate; and d) buffered salt solution, however, the Li declaration compares their adjuvant to aluminum hydroxide, which is insufficient because the adjuvant compared in the declaration is vastly different than metabolizable oil adjuvants or "SP Oil" as claimed.

Moreover, Applicant's declaration needs to be commensurate in scope with the claims. The MPEP states:

**DIRECT AND INDIRECT COMPARATIVE TESTS ARE PROBATIVE OF NONOBVIOUSNESS**

Evidence of unexpected properties may be in the form of a direct or indirect comparison of the claimed invention with the closest prior art which is commensurate in scope with the claims. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) and MPEP § 716.02(d) - § 716.02(e). See *In re Blondel*, 499 F.2d 1311, 1317, 182 USPQ 294, 298 (CCPA 1974) and *In re Fouche*, 439 F.2d 1237, 1241-42, 169 USPQ 429, 433 (CCPA 1971) for examples of cases where indirect comparative testing was found sufficient to rebut a prima facie case of obviousness. The patentability of an intermediate may be established by unexpected properties of an end product "when one of ordinary skill in the art would reasonably ascribe to a claimed intermediate the contributing cause' for such an unexpectedly superior activity or property." *In re Magerlein*, 602 F.2d 366, 373, 202 USPQ 473, 479 (CCPA 1979). "In order to establish that the claimed intermediate is a contributing cause' of the unexpectedly superior activity or property of an end product, an applicant must identify the cause of the unexpectedly superior activity or property (compared to the prior art) in the end product and establish a nexus for that cause between the intermediate and the end product." *Id.* at 479.

With regard to Point 2, contrary to Applicants assertion, it would have been expected, barring evidence to the contrary, that the composition would be effective in reducing shedding of *E. coli* O157:H7 because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed

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with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (KSR International Co. v. Teleflex inc., 500 U.S.-, 82 US{Q2d 1385 (2007). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obvious. See the recent Board decision *Ex parte Smith*,-- *USPQ2d*--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 *USPQ2d* at 1396).

With regard to Point 3, contrary to Applicant's arguments, the combination of references renders the instant composition obvious because they both teach the combination of components as claimed (i.e. components (a)-(d) and an aluminum hydroxide). Johnson et al. disclose a study to determine the effect of vaccinating dairy calves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of *Escherichia coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin. Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 50 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Moreover, Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprise antigens of inactivated cells from Gram negative bacteria such as

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*Escherichia coli* (see paragraph 0044). Moreover, the vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045).

Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066). Lastly, Saito et al. disclose using aluminum hydroxide in the disclosed composition (see paragraphs 0101 and 0109). Moreover, it would have been obvious to use the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response.

Limitations such as the amount of each component of the oil emulsion are being viewed as limitations of optimizing experimental parameters.

With regard to Point 4, Saito does not specifically disclose the combination of components, however it would have been obvious to one of ordinary skill in the art to combine the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response. All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co. v Teleflex INC.*, 550 U.S., 82 USPQ2d 1385).

With regard to Point 5, contrary to Applicant's arguments, Baylor et al., was used solely as an evidentiary reference to demonstrate that aluminum hydroxide has been

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commonly used as an adjuvant in many vaccines for decades and have been proven safe, as acknowledged in the Li declaration.

As previously presented, Johnson et al. disclose a study to determine the effect of vaccinating dairy calves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of *Escherichia coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin. Moreover, Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 50 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Johnson et al. does not specifically disclose an adjuvant comprising SP oil and aluminum hydroxide.

Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprise antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* (see paragraph 0044). Moreover, the vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066).



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It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Johnson et al. with the teachings of Saito et al. because Saito et al. disclose a vaccine which comprises inactivated cells of *E. coli* antigen coupled with an adjuvant comprising the components of SP oil. Further, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Johnson et al. with the teachings of Saito et al. to use inactivated whole *E. coli* O157:H7 because it is highly potent and can cause severe infections. It would have been obvious to use the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response. As evidenced by Baylor et al., which disclose that aluminum hydroxide has been commonly used as an adjuvant in many vaccines for decades and have been proven safe (see abstract and page S21-Summary).

It would have been expected, barring evidence to the contrary, that the composition would be effective in reducing shedding of *E. coli* O157:H7 because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (*KSR International Co. v. Teleflex inc.*, 500 U.S.-, 82 US{Q2d 1385 (2007)). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obvious. See the recent Board decision *Ex parte Smith*,--USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ2d at 1396).

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The method of the prior art is the same as that which has been claimed, consequently, the method necessarily produces minimal injection site reaction.

2. The rejection of claims 22-24 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Effect of dairy calves with an inactivated *E. coli* O157:H7 bacterin on shedding of *E. coli* O157:H7, 1999; Abstract 40 aP), in view of Saito et al. (U.S. 2005/0158330 A1), in view of Baylor et al. (Vaccine, 2002; 20: S18-S23) as set forth above and further in view of Elder et al. (Journal of Animal Science, 2002; 80 (sup. 1): 151 (abstract 602)) is maintained for the reasons set forth in the previous Office action.

Applicant argues that:

1) Elder does not cure any of the noted deficiencies of Johnson, Saito and/or Baylor.

Applicant's arguments have been considered, but are not persuasive.

The rejected claims are drawn to a method for reducing shedding of *E. coli* O157:H7 in an animal which comprises administering by parenteral injection to the animal an effective amount of a vaccine composition, wherein the vaccine composition comprises inactivated or killed *E. coli* O157:H7, an adjuvant and aluminum hydroxide, and optionally a pharmaceutically acceptable carrier; wherein said adjuvant is an oil emulsion comprising:

- a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer;
- b) 2% to 6% vol/vol of squalene;
- c) 0.1% to 0.5% vol/vol of polyoxyethylene sorbitan monooleate; and

d) buffered salt solution.

Subsequent claim 23 is drawn to a method that further comprises administering an effective amount of *Lactobacillus acidophilus* or neomycin medicated feed supplement to the animal.

With regard to Point 1, contrary to Applicant's assertion, Elder et al. disclose an intervention to reduce fecal shedding of *E. coli* O157:H7 in naturally infected cattle when administered neomycin (see page 151, abstract 602). Moreover, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the teachings of Johnson et al., Saito et al., and Baylor et al. with the teachings of Elder et al. because it is obvious to combine two compositions (neomycin and inactivated or killed whole *E. coli* O157:H7) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Providing the composition as a medicated feed would be obvious because it provides a more convenient means of delivery and would be more suitable for the improvement of intestinal function when fed to dairy animals such as cows, goats and ewes.

As previously presented, Johnson et al., Saito et al., and Baylor et al. disclose the limitations of claims 22 and 24 above. Johnson et al., Saito et al., and Baylor et al. do not specifically disclose that the method further comprises administering an effective amount of *Lactobacillus acidophilus* or neomycin medicated feed to the animal.

As set forth above, Johnson et al. disclose a study to determine the effect of vaccinating dairy calves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of *Escherichia coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin. Moreover, Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 0 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Johnson et al. does not specifically disclose an adjuvant comprising SP oil and aluminum hydroxide or the optional pharmaceutically acceptable carrier.

Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), a non-ionic surfactant, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprises antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* etc. (see paragraph 0044). The vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Moreover, Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066).

Saito et al. do not specifically disclose the use of aluminum hydroxide.

Elder et al. disclose an intervention to reduce fecal shedding of *E. coli* O157:H7 in naturally infected cattle when administered neomycin (see page 151, abstract 602).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the teachings of Johnson et al., Saito et al., and Baylor et al. with the teachings of Elder et al. because it is obvious to combine two compositions (neomycin and inactivated or killed whole *E. coli* O157:H7) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Providing the composition as a medicated feed would be obvious because it provides a more convenient means of delivery and would be more suitable for the improvement of intestinal function when fed to dairy animals such as cows, goats and ewes.

It would have been expected, barring evidence to the contrary, that the composition would be effective because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (*KSR International Co. v. Teleflex inc.*, 500 U.S.-, 82 USQ2d 1385 (2007). Moreover, *KSR* forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*,-- *USPQ2d*--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 *USPQ2d* at 1396).

***Conclusion***

3. No claim is allowed.
4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT  
1/2/08

/Robert A. Zeman/

for Lakia J. Tongue, Examiner of Art Unit 1645